Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

MFOLFOX6+PEMB Regimen

Folinic Acid (Leucovorin)-Fluorouracil-Oxaliplatin-Pembrolizumab

Disease Site

Gastrointestinal
- Esophagus
- Gastric / Stomach

Intent

Palliative

Regimen Category

Evidence-informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

This **Regimen Abstract** is an **abbreviated** version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Rationale and Uses

First-line treatment in patients with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative esophageal adenocarcinoma or squamous cell carcinoma, gastric adenocarcinoma or gastroesophageal junction (GEJ) adenocarcinoma.

(Refer to NDFP eligibility form for detailed funding criteria.)

Supplementary Public Funding	**pembrolizumab** New Drug Funding Program (Pembrolizumab - First-line Treatment of Advanced HER2-negative Esophageal, Gastric, and Esophagogastric Junction Carcinoma) (NDFP Website)

back to top

B - Drug Regimen

Pembrolizumab every 6 weeks:

pembrolizumab[1,2]	4 mg /kg	IV (max 400 mg)	Day 1; Every 6 weeks

And mFOLFOX6 every 2 weeks:

oxaliplatin	85 mg /m²	IV	Day 1
leucovorin	400 mg /m²	IV (concurrently with oxaliplatin)	Day 1
fluorouracil	400 mg /m²	IV bolus, after leucovorin	Day 1

Then,

fluorouracil	2400 mg /m²	IV continuous infusion over 46 hours (single dose)	Start on Day 1

[1]Dosing based on NDFP funding criteria. Alternative pembrolizumab dosing schedule is 2 mg/kg IV (max 200 mg) q3 weeks.

[2]Give pembrolizumab before chemotherapy when given on the same day.

back to top

C - Cycle Frequency

MFOLFOX6: Repeat every 2 weeks
Until disease progression or unacceptable toxicity^

PEMBROLIZUMAB: Repeat every 6 weeks (4 mg/kg dose)
Until disease progression or unacceptable toxicity, or up to a maximum of 2 years, whichever occurs first

^If chemotherapy is discontinued after at least 1 cycle due to intolerance, pembrolizumab may be continued as single agent (PEMB(MNT)) for up to 2 years, unless disease progression or unacceptable toxicity.

Refer to NDFP form for funding criteria for retreatment.

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

- Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Pembrolizumab Premedication (prophylaxis for infusion reactions):

- Routine pre-medication is not recommended.
- May consider antipyretic and H1-receptor antagonist in patients who experienced a grade 1-2 infusion reaction.

Oxaliplatin Premedication (prophylaxis for infusion reactions):

- There is insufficient evidence that routine prophylaxis with pre-medications reduces IR rates.
- Consider corticosteroids and H1-receptor antagonists ± H2-receptor antagonists in high-risk patients (i.e. ≥ cycle 6, younger age, female gender, prior platinum exposure, platinum-free interval ≥ 3 years).

Other Supportive Care:

- Avoid the use of corticosteroids or immunosuppressants before starting pembrolizumab treatment.
- Avoid mucositis prophylaxis with ice chips as cold temperatures can precipitate or exacerbate acute neurological symptoms of oxaliplatin.

back to top

J - Administrative Information

Approximate Patient Visit	3 to 4 hours
Pharmacy Workload (average time per visit)	49.356 minutes
Nursing Workload (average time per visit)	79.167 minutes

back to top

K - References

Al-Batran SE, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol 2008;26(9):1435-42.

Canada's Drug Agency. Reimbursement Recommendation: Pembrolizumab (Keytruda). Canadian Journal of Health Technologies. October 2024.

Fluorouracil drug monograph. Ontario Health (Cancer Care Ontario).

Oxaliplatin drug monograph. Ontario Health (Cancer Care Ontario).

pCODR reimbursement review (pembrolizumab: esophageal carcinoma, gastroesophageal junction adenocarcinoma). February 2022.

Pembrolizumab drug monograph. Ontario Health (Cancer Care Ontario).

Rha SY, Oh DY, Yañez P, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. Lancet Oncol 2023 Nov;24(11):1181-95. doi: 10.1016/S1470-2045(23)00515-6.

Sun JM, Shen L, Shah MA, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. Lancet 2021;398(10302):759-71. doi: 10.1016/S0140-6736(21)01234-4.

January 2025 Updated Rationale and Uses, Supplemental Public Funding, Drug Regimen, and Cycle Frequency sections

back to top

L - Other Notes

DPD Deficiency Testing and Guidance

Patients should be tested for DPD deficiency before starting treatment with fluorouracil. Refer to the DPD Deficiency Guidance for Clinicians for more information.

In patients with unrecognized DPD deficiency, acute, life-threatening toxicity may occur; if acute grade 2-4 toxicity develops, treatment should be stopped immediately and permanent discontinuation considered based on clinical assessment of the toxicities.

Antidote for Fluorouracil Overdose:

Uridine triacetate is a prodrug of uridine and is a specific antidote for treating fluorouracil overdose or severe early onset toxicities. If available, consider administering as soon as possible (i.e. within 96 hours) for suspected overdose. If not available, treatment is symptomatic and supportive.

For usage approval and supply, contact Health Canada's Special Access Program (SAP) (Phone: 613-941-2108. On-call service is available for emergencies).

The recommended dosing and administration for **uridine triacetate** in patients ≥18 years is:

- 10 grams (1 packet of coated granules) orally every 6 hours for 20 doses in total, without regards to meals.
- Granules should not be chewed. They should be mixed with 3 to 4 ounces of soft foods such as applesauce, pudding or yogurt.
- The dose should be ingested within 30 minutes of preparation, followed by at least 4 ounces of water.
- Refer to the prescribing information on dose preparation for NG-tube or G-tube use.

Additional resources on the management of fluorouracil infusion overdose:

- Management of Fluorouracil Infusion Overdose Guideline (Alberta Health Services)
- Management of Fluorouracil Infusion Overdose at the BCCA - Interim Guidance (BC Cancer Agency)

back to top

M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary's content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.

back to top